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What is claimed is:

- 5 1. An isolated nucleic acid molecule encoding a Y4
 receptor.
2. An isolated nucleic acid molecule of claim 1,
 wherein the nucleic acid molecule is a DNA
 molecule.
- 10 3. An isolated DNA molecule of claim 2, wherein the
 DNA molecule is a cDNA molecule.
4. An isolated DNA molecule of claim 2, wherein the
15 DNA molecule is a genomic DNA molecule.
5. An isolated nucleic acid molecule of claim 1,
 wherein the nucleic acid molecule is an RNA
 molecule.
- 20 6. An isolated nucleic acid of claim 1 wherein the
 nucleic acid molecule encodes a human Y4
 receptor.
- 25 7. An isolated nucleic acid molecule of claim 6
 wherein the nucleic acid molecule encodes a
 receptor being characterized by an amino acid
 sequence in the transmembrane region, wherein
 the amino acid sequence has 60% homology or
30 higher to the amino acid sequence in the
 transmembrane region of the human Y4 receptor
 shown in Figure 2.
- 35 8. An isolated nucleic acid molecule of claim 6
 wherein the human Y4 receptor has substantially
 the same amino acid sequence as shown in Figure
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9. An isolated nucleic acid molecule of claim 6 wherein the human Y4 receptor has the amino acid sequence as shown in Figure 1.
- 5 10. An isolated nucleic acid of claim 1 wherein the nucleic acid molecule encodes a rat Y4 receptor.
11. An isolated nucleic acid molecule of claim 10 wherein the rat Y4 receptor has substantially
10 the same amino acid sequence as shown in Figure 3.
12. An isolated nucleic acid of claim 10 wherein the
15 rat Y4 receptor has the amino acid sequence shown in Figure 3.
13. A purified Y4 receptor protein.
14. A vector comprising the nucleic acid molecule of
20 claim 1.
15. A vector comprising the nucleic acid molecule of claim 6.
- 25 16. A vector comprising the nucleic acid molecule of claim 10.
17. A vector of claim 14 adapted for expression in a
30 bacterial cell which comprises the regulatory elements necessary for expression of the nucleic acid in the bacterial cell operatively linked to the DNA encoding the Y4 receptor as to permit expression thereof.
- 35 18. A vector of claim 14 adapted for expression in a yeast cell which comprises the regulatory elements necessary for expression of the nucleic

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acid in the yeast cell operatively linked to the nucleic acid encoding the Y4 receptor as to permit expression thereof.

- 5 19. A vector of claim 14 adapted for expression in an insect cell which comprises the regulatory elements necessary for expression of the nucleic acid in the insect cell operatively linked to the nucleic acid encoding the Y4 receptor as to permit expression thereof.
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20. A vector of claim 19 wherein the vector is a baculovirus.
- 15 21. A vector of claim 14 adapted for expression in a mammalian cell which comprises the regulatory elements necessary for expression of the nucleic acid in the mammalian cell operatively linked to the nucleic acid encoding the Y4 receptor as to permit expression thereof.
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22. A vector of claim 15 adapted for expression in a mammalian cell which comprises the regulatory elements necessary for expression of the nucleic acid in the mammalian cell operatively linked to the nucleic acid encoding the Y4 receptor as to permit expression thereof.
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23. A vector of claim 22 wherein the vector is a plasmid.
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24. The plasmid of claim 23 designated pcEXV-Y4 (ATCC Accession No. 75631).
- 35 25. A vector of claim 16 adapted for expression in a mammalian cell which comprises the regulatory elements necessary for expression of the nucleic

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acid in the mammalian cell operatively linked to the nucleic acid encoding the Y4 receptor as to permit expression thereof.

- 5 26. A vector of claim 25 wherein the vector is a plasmid.
27. The plasmid of claim 26 designated pcEXV-rY4 (ATCC Accession No.).
- 10 28. A mammalian cell comprising the vector of claim 23 or 26.
29. A cell of claim 28 wherein the cell is non-neuronal in origin.
- 15 30. A cell of claim 28 wherein the cell is a COS-7 cell.
31. A cell of claim 27 wherein the cell is an LM(tk-) cell.
- 20 32. The cell of claim 31 designated L-hY4-3 (ATCC Accession No.).
- 25 33. A cell of claim 27 wherein the cell is an NIH-3T3 cell.
34. The cell of claim 33 designated N-hY4-5 (ATCC Accession No.).
- 30 35. A nucleic acid probe comprising a nucleic acid molecule of at least 15 nucleotides capable of specifically hybridizing with a unique sequence included within the sequence of a nucleic acid molecule encoding a Y4 receptor of claim 1.
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36. A nucleic acid probe of claim 35 wherein the nucleic acid encodes a human Y4 receptor.
- 5 37. A nucleic acid probe of claim 35 wherein the nucleic acid encodes a rat Y4 receptor.
38. The nucleic acid probe of claim 35 wherein the nucleic acid is DNA.
- 10 39. The nucleic acid probe of claim 35 wherein the nucleic acid is RNA.
40. An antisense oligonucleotide having a sequence capable of specifically hybridizing to an mRNA molecule encoding a Y4 receptor of claim 5 so as to prevent translation of the mRNA molecule.
- 15 41. An antisense oligonucleotide having a sequence capable of specifically hybridizing to the cDNA molecule of claim 3.
- 20 42. An antisense oligonucleotide of either of claims 40 or 41 comprising chemical analogues of nucleotides.
- 25 43. An antibody capable of binding to a Y4 receptor of claim 1.
44. An antibody of claim 43, wherein the Y4 receptor is a human Y4 receptor.
- 30 45. An antibody of claim 43, wherein the Y4 receptor is a rat Y4 receptor.
- 35 46. An antibody capable of competitively inhibiting the binding of the antibody of claim 43 to a Y4 receptor.

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47. An antibody of claim 43, wherein the antibody is a monoclonal antibody.
- 5 48. A monoclonal antibody of claim 47 directed to an epitope of a Y4 receptor present on the surface of a Y4 receptor expressing cell.
- 10 49. A pharmaceutical composition comprising an amount of the oligonucleotide of claim 40 effective to decrease activity of a Y4 receptor by passing through a cell membrane and binding specifically with mRNA encoding a Y4 receptor in the cell so as to prevent its translation and a pharmaceutically acceptable carrier capable of passing through a cell membrane.
- 15 50. A pharmaceutical composition of claim 49, wherein the oligonucleotide is coupled to a substance which inactivates mRNA.
- 20 51. A pharmaceutical composition of claim 50, wherein the substance which inactivates mRNA is a ribozyme.
- 25 52. A pharmaceutical composition of claim 49, wherein the pharmaceutically acceptable carrier comprises a structure which binds to a receptor on a cell capable of being taken up by cells after binding to the structure.
- 30 53. A pharmaceutical composition of claim 52 wherein the structure of the pharmaceutically acceptable carrier is capable of binding to a receptor which is specific for a selected cell type.
- 35 54. A pharmaceutical composition which comprises an amount of the antibody of claim 43 effective to

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block binding of a ligand to a Y4 receptor and a pharmaceutically acceptable carrier.

- 5 55. A transgenic nonhuman mammal expressing nucleic acid encoding a Y4 receptor of claim 1.
- 10 56. A transgenic nonhuman mammal comprising a homologous recombination knockout of the native Y4 receptor.
- 15 57. A transgenic nonhuman mammal whose genome comprises antisense nucleic acid complementary to nucleic acid encoding a Y4 receptor of claim 1 so placed as to be transcribed into antisense mRNA which is complementary to mRNA encoding a Y4 receptor and which hybridizes to mRNA encoding a Y4 receptor thereby reducing its translation.
- 20 58. The transgenic nonhuman mammal of either of claims 55 or 57, wherein the nucleic acid encoding a Y4 receptor additionally comprises an inducible promoter.
- 25 59. The transgenic nonhuman mammal of either of claims 55 or 57, wherein the encoding a Y4 receptor additionally comprises tissue specific regulatory elements.
- 30 60. A transgenic nonhuman mammal of any of claims 55, 56 or 57, wherein the transgenic nonhuman mammal is a mouse.
- 35 61. A method for determining whether a ligand can specifically bind to a Y4 receptor which comprises contacting a cell transfected with and expressing nucleic acid encoding the Y4 receptor

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of claim 1 with the ligand under conditions
permitting binding of ligands to such receptor,
and detecting the presence of any such ligand
bound specifically to the Y4 receptor, thereby
determining whether the ligand binds
specifically to a Y4 receptor.

62. A method of claim 61 wherein the Y4 receptor is
a human Y4 receptor.

63. A method of claim 61 wherein the Y4 receptor is
a rat Y4 receptor.

64. A method for determining whether a ligand can
specifically bind to a Y4 receptor which
comprises contacting a cell transfected with and
expressing nucleic acid encoding the Y4 receptor
of claim 1 with the ligand under conditions
permitting binding of ligands to such receptor,
and detecting the presence of any such ligand
bound specifically to the Y4 receptor, thereby
determining whether the ligand binds
specifically to a Y4 receptor, wherein the Y4
receptor is characterized by an amino acid
sequence in the transmembrane region, such amino
acid sequence having 60% homology or higher to
the amino acid sequence in the transmembrane
region of the human Y4 receptor shown in Figure
2.

65. A method of claim 64 wherein the Y4 receptor is
a human Y4 receptor.

66. A method of claim 64 wherein the Y4 receptor is
a rat Y4 receptor.

67. A method for determining whether a ligand can

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bind specifically to a Y4 receptor which comprises preparing a cell extract from cells transfected with and expressing nucleic acid encoding the Y4 receptor of claim 1, isolating a membrane fraction from the cell extract, contacting the ligand with the membrane fraction under conditions permitting binding of ligands to such receptor, and detecting the presence of any ligand bound to the Y4 receptor, thereby determining whether the compound is capable of specifically binding to a Y4 receptor.

68. A method of claim 67 wherein the Y4 receptor is a human Y4 receptor

69. A method of claim 67 wherein the Y4 receptor is a rat Y4 receptor.

70. A method of any of claims 61, 62, 63, 64, 65, 66, 67, 68, or 69 wherein the ligand is not previously known.

71. A ligand determined by the method of claim 70.

72. A method for determining whether a ligand is a Y4 receptor agonist which comprises contacting a cell transfected with and expressing nucleic acid encoding a Y4 receptor with the ligand under conditions permitting the activation of a functional Y4 receptor response from the cell, and detecting by means of a bioassay, such as a second messenger response, an increase in Y4 receptor activity, thereby determining whether the ligand is a Y4 receptor agonist.

73. A method for determining whether a ligand is a Y4 receptor agonist which comprises preparing a

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cell extract from cells transfected with and
expressing nucleic acid encoding a Y4 receptor
of claim 1, isolating a membrane fraction from
the cell extract, contacting the membrane
fraction with the ligand under conditions
permitting the activation of a functional Y4
receptor response and detecting by means of a
bioassay, such as a second messenger response,
an increase in Y4 receptor activity, thereby
determining whether the ligand is a Y4 receptor
agonist.

74. A method of either of claims 72 or 73 wherein
the Y4 receptor is a human Y4 receptor.

75. A method of either of claims 72 or 73 wherein
the Y4 receptor is a rat Y4 receptor.

76. A method for determining whether a ligand is a
Y4 receptor antagonist which comprises
contacting a cell transfected with and
expressing nucleic acid encoding a Y4 receptor
of claim 1 with the ligand in the presence of a
known Y4 receptor agonist, such as PP, under
conditions permitting the activation of a
functional Y4 receptor response and detecting by
means of a bioassay, such as a second messenger
response, a decrease in Y4 receptor activity,
thereby determining whether the ligand is a Y4
receptor antagonist.

77. A method for determining whether a ligand is a
Y4 receptor antagonist which comprises preparing
a cell extract from cells transfected with and
expressing nucleic acid encoding a Y4 receptor
of claim 1, isolating a membrane fraction from
the cell extract, contacting the membrane

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fraction of the extract with the ligand in the presence of a known Y4 receptor agonist, such as PP, under conditions permitting the activation of a functional Y4 receptor response and detecting by means of a bioassay, such as a second messenger response, a decrease in Y4 receptor activity, thereby determining whether the ligand is a Y4 receptor antagonist.

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- 10 78. A method of either of claims 76 or 77 wherein the Y4 receptor is a human Y4 receptor.
- 15 79. A method of either of claims 76 or 77 wherein the Y4 receptor is a rat Y4 receptor.
80. A method of any of claims 72, 73, 76 or 77 wherein the second messenger assay comprises measurement of intracellular cAMP.
- 20 81. A method of any of claims 72, 73, 76, or 77 wherein the second messenger assay comprises measurement of intracellular calcium mobilization.
- 25 82. A method of any of claims 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78 or 79 wherein the cell is a mammalian cell.
- 30 83. The method of claim 82 wherein the mammalian cell is nonneuronal in origin.
84. A method of claim 83, wherein the mammalian cell is nonneuronal in origin is a COS-7 cell.
- 35 85. A method of claim 83, wherein the mammalian cell nonneuronal in origin is a CHO cell.

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86. A method of claim 83, wherein the mammalian cell nonneuronal in origin is a LM(tk-) cell.
87. A method of claim 83, wherein the mammalian cell nonneuronal in origin is a NIH-3T3 cell.
88. A ligand detected by the method of any of claims 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80 or 81.
89. A ligand of claim 88 wherein the ligand is not previously known.
90. A pharmaceutical composition which comprises an amount of a Y4 receptor agonist determined by the method of either of claims 72 or 73 effective to reduce activity of a Y4 receptor and a pharmaceutically acceptable carrier.
91. A pharmaceutical composition of claim 90 wherein the Y4 receptor agonist is not previously known.
92. A pharmaceutical composition which comprises an amount of a Y4 receptor antagonist determined by the method of either of claims 76 or 77 effective to increase activity of Y4 receptor and a pharmaceutically acceptable carrier.
93. A pharmaceutical composition of claim 92 wherein the Y4 receptor antagonist is not previously known.
94. A method of screening drugs to identify drugs which specifically bind to a Y4 receptor on the surface of a cell which comprises contacting a cell transfected with and expressing nucleic acid encoding a Y4 receptor with a plurality of

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drugs under conditions permitting binding of drugs to the Y4 receptor, and determining those drugs which specifically bind to the transfected cell, thereby identifying drugs which specifically bind to a Y4 receptor.

95. A method of screening drugs to identify drugs which specifically bind to a Y4 receptor on the surface of a cell which comprises preparing a cell extract from cells transfected with and expressing nucleic acid encoding a Y4 receptor, isolating a membrane fraction from the cell extract, contacting the membrane fraction with a plurality of drugs, and determining those drugs which bind to the transfected cell, thereby identifying drugs which specifically bind to a Y4 receptor.
96. A method of either of claims 94 or 95 wherein the Y4 receptor is a human Y4 receptor.
97. A method of either of claims 94 or 95 wherein the Y4 receptor is a rat Y4 receptor.
98. A method of screening drugs to identify drugs which act as agonists of Y4 receptor which comprises contacting a cell transfected with and expressing nucleic acid encoding a Y4 receptor with a plurality of drugs under conditions permitting the activation of a functional Y4 receptor response, and determining those drugs which activate such receptor using a bioassay such, as a second messenger assay, thereby identifying drugs which act as Y4 receptor agonists.
99. A method of screening drugs to identify drugs

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which act as agonists of Y4 receptor which comprises preparing a cell extract from cells transfected with and expressing nucleic acid encoding a Y4 receptor, isolating a membrane fraction from the cell extract, contacting the membrane fraction with a plurality of drugs under conditions permitting the activation of a functional Y4 receptor response, and determining those drugs which activate such receptor using a bioassay, such as a second messenger assay, thereby identifying drugs which act as Y4⁺ receptor agonists.

100. A method of either of claims 98 or 99 wherein the Y4 receptor is a human Y4 receptor.

101. A method of either of claims 98 or 99 wherein the Y4 receptor is a rat Y4 receptor.

102. A method of screening drugs to identify drugs which act as Y4 receptor antagonists which comprises contacting a cell transfected with and expressing nucleic acid encoding a Y4 receptor with a plurality of drugs in the presence of a known Y4 receptor agonist, such as PP, under conditions permitting the activation of a functional Y4 receptor response, and determining those drugs which inhibit the activation of the receptor using a bioassay, such as a second messenger assay, thereby identifying drugs which act as Y4 receptor antagonists.

103. A method of screening drugs to identify drugs which act as Y4 receptor antagonists which comprises preparing a cell extract from cells transfected with and expressing nucleic acid encoding a Y4 receptor, isolating a membrane

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fraction from the cell extract, contacting the membrane fraction with a plurality of drugs in the presence of a known Y4 receptor agonist, such as PP, under conditions permitting the activation of a functional Y4 receptor response, and determining those drugs which inhibit the activation of the receptor using a bioassay, such as a second messenger assay, thereby identifying drugs which act as Y4 receptor antagonists.

104. A method of either of claims 102 or 103 wherein the Y4 receptor is a human Y4 receptor.

105. A method of either of claims 102 or 103 wherein the Y4 receptor is a rat Y4 receptor.

106. A method of any of claims 98, 99, 102 or 103 wherein the second messenger assay comprises measurement of intracellular cAMP.

107. A method of any of claims 98, 99, 102 or 103 wherein the second messenger assay comprises measurement of intracellular calcium mobilization.

108. The method of any of claims 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, or 105 wherein the cell is a mammalian cell.

109. The method of claim 108 wherein the mammalian cell is nonneuronal in origin.

110. The method of claim 109 wherein the mammalian cell nonneuronal in origin is a Cos-7 cell.

111. The method of claim 109 wherein the mammalian cell is nonneuronal in origin.

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cell nonneuronal in origin is a CHO cell.

112. The method of claim 109 wherein the mammalian cell nonneuronal in origin is a LM(tk-) cell.

113. The method of claim 109 wherein the mammalian cell nonneuronal in origin is an NIH-3T3 cell.

114. A pharmaceutical composition comprising a drug identified by the method of either of claims 98 or 99 and a pharmaceutically acceptable carrier.

115. A pharmaceutical composition comprising a drug identified by the method of either of claims 102 or 103 and a pharmaceutically acceptable carrier.

116. A method of detecting expression of a Y4 receptor by detecting the presence of mRNA coding for a Y4 receptor which comprises obtaining total mRNA from the cell and contacting the mRNA so obtained with the nucleic acid probe of claim 40 under hybridizing conditions, and detecting the presence of mRNA hybridized to the probe, thereby detecting the expression of a Y4 receptor by the cell.

117. A method of treating an abnormality in a subject, wherein the abnormality is alleviated by decreasing the activity of a Y4 receptor which comprises administering to a subject an effective amount of the pharmaceutical composition of either of claims 90 or 114, thereby treating the abnormality.

118. A method of treating an abnormality in a subject wherein the abnormality is alleviated by

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decreasing the activity of Y4 receptor which comprises administering to a subject an effective amount of a Y4 receptor antagonist determined by the methods of any of claims 76, 77, 102, or 103, thereby treating the abnormality.

119. The method of either of claims 117 or 118 wherein the abnormal condition is amnesia.
120. The method of either of claims 117 or 118 wherein the abnormal condition is a feeding disorder.
121. The method of either of claims 117 or 118 wherein the abnormal condition is epilepsy.
122. The method of either of claims 117 or 118 wherein the abnormal condition is hypertension.
123. The method of either of claims 117 or 118 wherein the abnormal condition is sleeping disorder.
124. The method of either of claims 117 or 118 wherein the abnormal condition is pain.
125. A method of treating an abnormality in a subject, wherein the abnormality is alleviated by decreasing the activity of a human Y4 receptor which comprises administering to the subject an amount of the pharmaceutical composition of claim 54 effective to block binding of ligands to a Y4 receptor, thereby treating the abnormality.
126. A method of treating an abnormality in a

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subject, wherein the abnormality is alleviated by decreasing the activity of a human Y4 receptor which comprises administering to the subject an effective amount of the pharmaceutical composition of claim 49, thereby treating the abnormality.

127. The method of either of claims 125 or 126 wherein the abnormal condition is amnesia.

128. The method of either of claims 125 or 126 wherein the abnormal condition is a feeding disorder.

129. The method of either of claims 125 or 126 wherein the abnormal condition is epilepsy.

130. The method of either of claims 125 or 126 wherein the abnormal condition is hypertension.

131. The method of either of claims 125 or 126 wherein the abnormal condition is sleeping disorder.

132. The method of either of claims 125 or 126 wherein the abnormal condition is pain.

133. A method of detecting the presence of a Y4 receptor on the surface of a cell which comprises contacting the cell with the antibody of claim 43 under conditions permitting binding of the antibody to the receptor, and detecting the presence of the antibody bound to the cell, thereby detecting the presence of a Y4 receptor on the surface of the cell.

134. A method of determining the physiological

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effects of expressing varying levels of Y4 receptors which comprises producing a transgenic nonhuman mammal of claim 55 whose levels of Y4 receptor expression are varied by use of an inducible promoter which regulates Y4 receptor expression.

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135. A method of determining the physiological effects of expressing varying levels of Y4 receptors which comprises producing a panel of transgenic nonhuman mammals of claim 55 each expressing a different amount of Y4 receptor.

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136. A method for identifying a Y4 receptor antagonist capable of alleviating an abnormality in a subject, wherein the abnormality is alleviated by decreasing the activity of a Y4 receptor which comprises administering the antagonist to a transgenic nonhuman mammal of any of claims 55, 57, 58, 59 or 60 and determining whether the antagonist alleviates the physical and behavioral abnormalities displayed by the transgenic nonhuman mammal as a result of activity of a Y4 receptor, thereby identifying a Y4 antagonist.

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137. An antagonist identified by the method of claim 136.

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138. A pharmaceutical composition comprising an antagonist identified by the method of claim 136 and a pharmaceutically acceptable carrier.

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139. A method of treating an abnormality in a subject wherein the abnormality is alleviated by decreasing the activity of a Y4 receptor which comprises administering to the subject an

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effective amount of the pharmaceutical composition of claim 138, thereby treating the abnormality.

- 5 140. A method for identifying a Y4 receptor agonist capable of alleviating an abnormality in a subject wherein the abnormality is alleviated by activation of a Y4 receptor which comprises administering the agonist to the transgenic
10 nonhuman mammal of any of claims 55, 56, 57, 58, 59 or 60 and determining whether the substance alleviates the physical and behavioral abnormalities displayed by the transgenic nonhuman mammal, the alleviation of the
15 abnormality indicating the identification of a Y4 receptor agonist.
- 20 141. An agonist identified by the method of claim 140.
- 25 142. A pharmaceutical composition comprising an agonist identified by the method of claim 140 and a pharmaceutically acceptable carrier.
- 30 143. A method for treating an abnormality in a subject wherein the abnormality is alleviated by activation of a Y4 receptor which comprises administering to the subject an effective amount of the pharmaceutical composition of claim 142, thereby treating the abnormality.
- 35 144. A method for diagnosing a predisposition to a disorder associated with the activity of a specific Y4 receptor allele which comprises:
- a. obtaining DNA of subjects suffering from the disorder;

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- b. performing a restriction digest of the DNA with a panel of restriction enzymes;
 - c. electrophoretically separating the resulting DNA fragments on a sizing gel;
 - d. contacting the resulting gel with a nucleic acid probe capable of specifically hybridizing to DNA encoding a Y4 receptor and labelled with a detectable marker;
 - e. detecting labelled bands which have hybridized to the DNA encoding a Y4 receptor labelled with a detectable marker to create a unique band pattern specific to the DNA of subjects suffering from the disorder;
 - f. preparing DNA obtained for diagnosis by steps a-e; and
 - g. comparing the unique band pattern specific to the DNA of subjects suffering from the disorder from step e and the DNA obtained for diagnosis from step f to determine whether the patterns are the same or different and to diagnose thereby predisposition to the disorder if the patterns are the same.
145. The method of claim 144 wherein a disorder associated with the expression of a specific human Y4 receptor allele is diagnosed.
146. A method of preparing the purified isolated Y4 receptor of claim 13 which comprises:

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- 5 a. constructing a vector adapted for
expression in a cell which comprises the
regulatory elements necessary for the
expression of nucleic acid in the cell
operatively linked to the nucleic acid
encoding a Y4 receptor as to permit
expression thereof, wherein the cell is
selected from the group consisting of
bacterial cells, yeast cells, insect cells
10 and mammalian cells;
- b. inserting the vector of step a in a
suitable host cell;
- 15 c. incubating the cells of step b under
conditions allowing the expression of a Y4
receptor;
- d. recovering the receptor so produced; and
- 20 e. purifying the receptor so recovered,
thereby preparing an isolated Y4 receptor.